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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/943,446	08/30/2001	Tessa A. Castleberry	PC10891AGPR	9426

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EXAMINER	
JIANG, DONG	

ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/943,446	CASTLEBERRY ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *4-13 and 16-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,14 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/9/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicant's election with traverse of Group I invention, claims 1-3, 14 and 15, filed on 22 August 2003 is acknowledged. The traversal is on the ground(s) that it would not be an undue burden on the Examiner to search all of the claims of this application at once as all of the claims are drawn to the same protein, its encoding DNA, or method of using the same, and that at least the claims of Groups I and II should be combined as it clearly will be necessary to search using all of the polypeptide and polynucleotide sequence no matter which group is elected. This is not found persuasive because consistent with current patent practice, a serious burden may be established by (A) separate classification thereof; (B) a separate status in the art when they are classifiable together; or (C) a different field of search. In the instant case, Groups I-III are patentably distinct inventions as shown by their separate classification, indicating each distinct subject has attained recognition in the art as a separate subject for inventive effort, and also a separate field of search. As stated in the MPEP 803, "a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP 802.02". Further, a search of the elected Group I, directed to a polypeptide, does not necessarily require the search of the encoding DNA in order to find prior art in the instant case. A search of a polypeptide isolated from its natural source would not necessarily reveal information about the DNA encoding the polypeptide. Thus, searching the encoding DNA is a divergent and separate search, and would constitute undue burden.

The requirement is still deemed proper and is therefore made FINAL.

Currently, claims 1-18 are pending, and claims 1-3, 14 and 15 are under consideration. Claims 4-13 and 16-18 are withdrawn from further consideration as being drawn to a non-elected invention.

Objections and Rejections under 35 U.S.C. 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 14 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite for the recitation of "one *or more* conservative substitutions" in line 4. It is unclear what is the upper limitation of numbers of the amino acids for the substitution to take place, and whether it includes functional equivalent. The term "more" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In the instant case it is not clear as how many is "more". Given the broadest interpretation, it reads on an indefinite number of amino acid residues being substituted while retaining the biological property, up to and including replacement of the entire protein. The claim is further indefinite because the metes and bounds of "conservative substitutions" cannot be determined for the following reason. It is noted that the specification defines the term (at page 8) as "a substitution, addition, or deletion of an amino acid in a proteinaceous molecule that is not expected to significantly affect the activity of thereof", which is repugnant to the meaning of "conservative substitutions" known in the art as the art does not recognize that addition, or deletion of an amino acid in a protein is "conservative substitutions". The claim is further indefinite for the recitation of having "canine PTH1 activity" because it is unclear what it is meant. For instance, the ligand binding of the PTH1 receptor can be considered PTH1 activity, however, depending upon the binding ligand, agonist or antagonist, the biological property medicated by the PTH1 can be completely different. As such, the metes and bounds of the claim cannot be determined.

Claim 2 is similarly indefinite for the recitation of "conservative substitutions".

The remaining claims are rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited in scope to an isolated proteinaceous molecule having SEQ ID NO:6, does not reasonably provide enablement for claims to proteinaceous molecule having SEQ ID NO:6 with "more conservative substitutions". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claim 1 is directed to a protein molecule having an amino acid sequence of SEQ ID NO:6, or thereof with one or more conservative substitutions while retaining canine PTH1 activity, which, given the broadest interpretation, reads on any or all possible functional equivalents of PTH1 because there is no upper limit as to how may amino acid residues can be substituted.

Enablement is not commensurate in scope with the claim to any or all possible proteins having canine PTH1 activity. It is noted that the patentability of the claimed variants rests not on the biological property, but rather the particular sequences disclosed in the specification as filed because of the existence of other distinct proteins with the same biological property. As there is no upper limit given on the number of amino acid changes, the claims read on, therefore, any functionally equivalent protein with no structure similarity to SEQ ID:6 actually required. Additionally, there is a lack of predictability in the prior art on the relationship of the function and structure of the PTH1 because of the lack of sequence identity, and the specification of the current application discloses only *one* PTH1, and it does not provide clear direction or enough guidance to teach how to make a commensurate number of the claimed species without altering the biological property. Based upon the very limited number of disclosed species, it is not at all predictable what essential structures are required for the protein to be functional, and it would require undue experimentation to determine such. As the specification does not teach how to make a number of species that would be commensurate in scope with the claim, it is found that it

would require undue experimentation to practice the invention in a manner commensurate in scope with the claim.

Due to the large quantity of experimentation necessary to make and test the claimed functional variants of the canine PTH1, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which embrace a broad class of structural variants, undue experimentation would be required of the skilled artisan to use the claimed invention in its full scope.

The Examiner notes that the description of claimed proteins via a biological function is similar to the situation in *Ex parte Maizel* (27 USPQ2d 1662 at 1665) in which it was found that:

> Appellants have not chosen to claim the DNA by what it is but, rather, by what it does, i.e., encoding either a protein exhibiting certain characteristics, *or* a biologically functional equivalent thereof. Appellants' claims might be analogized to a single means claim of the type disparaged by the Court of Customs and Patent Appeals in *In re Hyatt,* 708F.2d 712, 218 USPQ 195 (Fed. Cir. 1983). The problem with the phrase "biologically functional equivalent thereof" is that it covers any conceivable means, i.e., cell or DNA, which achieves the stated biological result while the specification discloses, at most, only a specific DNA segment known to the inventor. Clearly the disclosure is not commensurate in scope with the claims."

In the current instance, the claims do not positively identify the protein of the invention by its sequence, but rather define such in terms of its biological activity. Therefore, the currently pending claims are analogous to the DNA claims in *Maizel*, in which the DNA was defined by the biological activity of the protein it encoded.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by, or, in the alternative, under 35 U.S.C. 103(a) as obvious over Segre et al., US5,886,148.

Segre discloses a polypeptide sequence of a human PTH receptor (SEQ ID NO:21), which comprises 593 amino acids, and is 95.2% identical to SEQ ID NO:6 of the present invention (see computer printout of the search results). As such, Segre's sequence anticipates the sequence of claim 1 as it is a proteinaceous molecule comprising an amino acid sequence of SEQ ID NO:6 with one or more "conservative substitutions" (based on the definition in the specification, page 8). With respect to the limitation of "having canine PTH1 activity", given the fact of the high sequence homology between the prior art sequence and the instant SEQ ID NO:6, and between the human and the canine PTH, it is highly likely that Segre's human PTH receptor would inherently have canine PTH1 activity. In fact, it is certain that Segre's human PTH receptor would bind to a canine PTH1 antibody, which would meet the limitation of "having canine PTH1 activity". Additionally, the statement on page 2 of the specification further supports such inherency, as it indicates that "this receptor is similar to PTH1 receptors from human, mouse, and rat on the molecular level and has functional characteristics in common with these receptors with respect to ligand binding and activation". Therefore, the burden shifts to the applicant to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention. Note the case law of *In re Best* 195 USPQ 430, 433 (CCPA 1977).

Further, Segre teaches a composition comprising the human PTH receptor and a pharmaceutically acceptable carrier. Therefore, the reference also anticipates claim 14.

Conclusion:

Claims 3 and 15 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

Dong Jiang, Ph.D.
Patent Examiner
AU1646
5/10/04